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ON THE SO-CALLED MALIGNANT PUSTULE OF EXTERNAL ANTHRAX.

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BACTERIAL pathogeny is the youngest and not the least promising bud on the tree of pathology. The influence of vegetable micro-organisms in morbid processes engrosses considerable attention amongst medical men, and is steadily becoming more widely acknowledged. Of the group of diseases recognised as being associated with bacteria, *anthrax* appears to be the member which has been most fully and successfully studied. Therefore a survey of the present position of our knowledge of anthrax, so far as its external variety is concerned, may prove of interest and profit as affording some insight into the views of modern pathologists.

But the subject is additionally important because of its practical bearing. For though "malignant pustule" is comparatively unknown in this district, and the nature of the local industries considerably lessens the risk of its occurrence, yet in so large a centre of population, having wide commercial relations, we are every day exposed to the liability of being confronted with cases of this malady. And, be it remembered, the disease is one which is very fatal if left to nature, whereas early diagnosis and energetic surgical treatment almost, if not quite, invariably effect a cure. As giving point to the above observation, attention may be called to the recent outbreak of anthrax amongst cattle in Poulton, Gloucestershire, attended with loss of life in the person of a man who skinned a diseased carcase.*

The writer's interest in the subject was aroused during his studentship and house-surgeoncy at Guy's Hospital, where cases from time to time present themselves from the tanneries and leather manufactories of Bermondsey. He possesses notes of twenty-six cases which were treated in Guy's Hospital between 1873 (when the disease appears to have been noted for the first time) and 1883, access to the records having been kindly accorded.

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* Lancet, July 9, 1887.

Before proceeding with the biological and clinical features of "malignant pustule," a glance at the history of its literature may not be deemed uninteresting.

I. HISTORICAL.*

Anthracoid diseases in their several forms have been recognised from the earliest times, and no quarter of the globe is free from their ravages. Thus it is suggested by Bollinger that such an early record as Exodus ix. refers to anthrax; and with regard to geographical distribution, it is found in the polar regions (as Siberia and Lapland) and in the tropics (East and West Indies), as well as widely spread throughout Europe, America and Africa. In keeping with this antiquity and universality a confusing medley of terms has arisen, the external forms of the affection being variously named "*οἴδημα*," "sacer ignis," "pustula" (by the Greek and Roman veterinarians), "al Humrah" (= Persian fire), "Siberian boil," "charbon," "anthrax carbuncle," and "malignant pustule." The generic name anthrax has come to be applied to the typical disease, whether manifesting itself constitutionally, or locally in the skin; the latter variety, however, is best known in Britain as "malignant pustule," though the expression is a singularly unfortunate one, for the lesion is not malignant in the sense of having a connection with sarcoma or carcinoma, nor is it a pustule. The synonym "charbon" is less open to objection. If we may be permitted to coin a new term we would suggest "anthrax eschar" as denoting the condition more accurately.

Heusinger, in his elaborate monograph on "Milzbrand" (= anthracæmia) published at Erlangen in 1850, states that the Arabians were acquainted with the disease, and their writers have given a precise description of it as it affected man. During the middle ages the unity of the different forms was lost sight of, and it was not until Chabert wrote his treatise "*Du Charbon*" in 1780 that the matter was put in a clear light. Fournier published his "*Observations sur les charbons malins*" in 1757; but to Chabert is chiefly due the credit of proving the similarity of maladies which had previously been regarded as distinct, and his classification is still in use. His work ran through seven editions in seven years, and was translated into Spanish and Italian.

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* Compiled from Bollinger's article in Ziemssen's Medicine, and from various English publications since 1847.

The contagiousness of anthrax was observed and noted by Fournier, Bertin, Montfils, and other writers in the eighteenth century. Kausch, however, in 1805, whilst admitting the infection of men and animals by means of blood and flesh, maintained the theory of non-contagiousness in cattle. Delafond (1843), took much the same view with regard to ovine anthrax, which he regarded as an acute enteritis associated with blood changes; he came near the truth when he referred the chief cause to chemical conditions of the soil.

Gerlach (1845), established by experiment the contagiousness of the sheep-plague, whose identity with anthrax he also proved, and he came to the conclusion that the contagium was a very indestructible volatile body.

Heusinger (1850), promulgated the theory that the disease was a malarial neurosis. His views were shortly these—(1) a contagious poison is developed in local centres of disease and carried away in the blood; (2) the different forms in man and animals are identical; (3) the poison originates in herbivora, but all other animals may become infected. Virchow, in 1855, gave assent to the malarial theory, and expressed the opinion that the morbific principle was probably a ferment. He thus, remarkably enough, anticipated, before the true *materies morbi*—the bacillus anthracis—was made known, the latest accepted views that this organism gives rise to a fermentative action.

But the problem which had so long baffled investigators was already solved, and during this year (1855) the solution was made known in Casper's *Vierteljahrschrift*, by the publication of Pollender's epoch-making discoveries. As early as 1849, Pollender found that the blood of cattle suffering from anthrax contained a countless mass of fine rod-like bodies, apparently of a vegetable nature. This is remarkable as the first discovery of specific organisms in morbid blood. A new epoch was thus inaugurated by the powerful impetus given to the study of the vast and but little explored field of comparative pathology. Independently of Pollender the rods were found by Brauell (1857) in the blood of men, horses, and sheep, after death from anthrax. As the result of his experiments he arrived at these conclusions :—(1) The rods were vibriones ; (2) they appeared from one to ten hours before death, but were wanting in the blood of convalescing animals ; (3) blood which did not seem to contain them, might nevertheless produce the disease ; (4) they were, therefore, of diagnostic and prognostic value, but they did not constitute the poison of anthrax, nor were they the carriers of that poison. Delafond (1860) entirely coincided with these views : he thought the particles were a kind of leptothrix, whilst others considered them to be fibrin or blood-crystals.

The next work of consequence was that of Davaine, in 1863 ; he named the rods bacteridia to distinguish them from the bacteria of putrefaction, which were motile, and held that they were the poisonous principle by which anthrax is propagated. Dr. Budd* called attention in England to an important observation made by Davaine:—In April, 1864, Dr. Raimbert attended for " malignant pustule " a carter employed on a farm where there had been an outbreak of splenic fever. Dr. Davaine found in the "pustule" a felt-work of bacteridia, and he infected rabbits with splenic fever by feeding them with the morbid material. The identity of the anthrax of animals and malignant pustule of man was thus demonstrated. Davaine estimated the number of bacteridia in a single drop of blood at about ten millions ; he was able to produce the disease with the millionth dilution of such a drop. He further alleged that bacteridia were invariably present in anthrax, and that with their disappearance the blood ceased to be infectious.

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* Lancet, 1865. Dr. Budd displays a hopeful foresight in remarking—"perhaps we are on the eve of knowing, avoiding, and curing contagious scourges." A consummation devoutly to be wished !

These observations served as a new point of departure in the study of bacteria, and, owing chiefly to the researches of Ehrenberg and Nägeli, supplemented by those of Cohn, considerable light has been thrown upon the life-history of vegetable parasites, particularly of the family to which the anthrax bacillus belongs, namely, Schizomycetes or Bacteria, a sub-division of the Fungi. It is to Cohn that we are indebted for the term *bacillus anthracis*, to which Davaine's older name bacteridium has everywhere given place. The value of Davaine's work, however, has been lasting, and his propositions have been substantially confirmed by trustworthy researchers, as Bollinger and Koch in Germany, Toussaint and Pasteur in France, Klein and Greenfield in England.

Our own country has been conspicuously absent from the earlier part of the narrative. Nor is this surprising, for whereas anthrax is enzoötic throughout the pastoral regions of continental Europe, Great Britain is strikingly excepted. It hence follows that our knowledge of the disease is chiefly derived from French and German writers. In England the malady appears to have been first observed about 1840 among the woolsorters at Bradford, where it has been ever since endemic, and has acquired the name of "woolsorters' disease." The history of the disease in its connection with Bradford claims a brief notice.

According to Dr. Bell, alpaca and mohair were introduced into the district as textile materials about 1837, and the appearance of the disease is popularly supposed to date from this time. Occasional suspicious deaths occurred amongst the woolsorters without attracting much notice ; but when, as sometimes happened, several men working in the same room died within a short time of one another, the sorters would become alarmed. Years of increased fatality were 1846, 1854, 1867 and 1876.

The workmen came to look upon Van mohair, the fleece of a goat inhabiting the Van district of Asia Minor, as especially dangerous; and a custom arose at certain mills for employés to determine by drawing lots which of them should work upon it. Public concern slowly—fatally so—became aroused, and after men had gone on strike in 1880, the Local Government Board directed Mr. Spear to visit Bradford and report on the local disease. The combined investigations of Mr. Spear and Dr. Greenfield have conclusively proved the malady to be genuine anthrax.*

What remains to be told of the records in Britain can be summed up in a few words. In his translation of Chelius' *System of Surgery*, published in 1847, South refers to three cases of external anthrax. They were recorded by Mr. Lawrence as having occurred in an English hair-factory, and were called "malignant pustule." Next, the late Mr. Harvey Ludlow wrote an article on the subject in 1852,† and gave an account of cases treated in St. Bartholomew's Hospital. The diagnosis of these cases, however, appears to be open to question; a clear history of infection is wanting, and the clinical histories resemble those of carbuncle or poisoned wound. Ludlow was evidently familiar with the writings of the French anthracologists. His article is valuable as showing that attention was paid to the disease in England upwards of thirty years ago.

Undoubtedly the chief credit of bringing the external anthrax prominently under the notice of the profession in this country is due to Dr. William Budd, of Bristol. He read a paper on the subject before the British Medical Association in 1862. He then speaks of the affection as having been "hitherto unnoticed" in England; but he seems to have overlooked the cases by Lawrence and Ludlow. Dr. Budd collected nine cases, eight of which proved fatal. He strongly insisted on the history of infection, and asserted that the "pustule" is always derived from animals suffering from charbon, though it is communicable from man to man. He specifies four methods of contagion :—(i.) by direct inoculation, as in the case of herdsmen ; (ii.) by means of skins or hair ; (iii.) by the agency of flies or insects ; (iv.) by eating diseased flesh.

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* Local Government Board Medical Officer's Report, 1881.

† Medical Times and Gazette.

In this same year, 1862, a case in St. Bartholomew's Hospital under the care of Mr.—now Sir James—Paget was reported. It was diagnosed as "malignant pustule." In a prefatory note the fact is mentioned that the two largest meat markets in London—one for living the other for dead animals—were then near the Hospital.

An outbreak of anthrax in a horse-hair factory at Glasgow is described in a report to the Local Government Board by Dr. Russell in 1878.

At Guy's Hospital external anthrax has become a familiar disease. It has been known since 1873 at least, and upwards of thirty cases have been treated. The Guy's Surgeons, and particularly Mr. Davies-Colley, have rendered valuable service by repeatedly bringing the subject under the notice of the Medico-Chirurgical and other London Societies. There can be no doubt that the explanation of the comparative frequency with which this dangerous malady is observed at Guy's Hospital is to be found in the fact that large quantities of foreign fleeces, skins, and hides are imported into the adjacent district of Bermondsey for use in the extensive tanneries and leather manufactories.

II. ÆTIOLOGICAL.

We now proceed to consider the causation of the peculiar skin lesion of anthrax, and the constitutional symptoms thereon dependent. With this subject the life-history of the *bacillus anthracis* is so closely bound up, that it will be convenient in the present section to include some account of the characters and habits of the micro-organism; for the relationship subsisting between the parasite and the disease is now acknowledged by general consent to be that of cause and effect.

Happily, our enquiries under this head can be conducted in a literary atmosphere which is agreeably serene and refreshing, in comparison with the agitated and heated conditions prevalent during late years around the battle-grounds of tubercle, hydrophobia, and, most recently of all, scarlatina. It is a pleasing augury for other diseases embraced by bacteriology—which one may term the New Learning of pathology—that anthrax, after much fervid controversy, has passed beyond the stage of *quot homines tot sententiæ*, into one where something like unanimity prevails—at any rate so far as relates to causation, the question of prophylaxis being still a vexed one.

The evidence from which modern views of the ætiology of the disease have been constructed, is based partly on observation, partly on experiment. For the sake of clearness, the evidence will be split up, and the most important points dealt with seriatim.

1. *Geographical Distribution.*—'Malignant Pustule' is most frequently met with in districts where anthrax is enzoötic

amongst domestic animals. Certain affected parts of continental Europe suffer enormously from the yearly ravages of this highly contagious and deadly disease amongst sheep and horned cattle. It has been estimated that the loss incurred by the farmers in the country about Orleans alone amounted to three million francs in 1881, the mortality in the flocks being as high as 10 per cent.* M. Chamberland writes:—"In the department of Seine-et-Marne certain farms pay a heavy tribute every year to this plague; the districts of Provins, Fontainebleau, and Meaux, alway suffer severely; many farms in these districts go by the name of splenic-fever farms; the best farmers take them with fear and trembling. In the high lands of Auvergne, in Cantal for example, there are *montagnes maudites* (accursed hills), on which flocks lose 10 or 15 per cent. of their number, owing to anthrax (splenic-fever); nor need it astonish us to find that in this part of the country, the probability of the occurrence of anthrax is an element in the price of farms."†

In South Africa, during the Zulu war, an extremely fatal outbreak occurred amongst the horses and oxen; in some places upwards of 50 per cent. were destroyed per week.

Saxony, Hungary, the districts of the lower Danube, parts of Russia, and of North America, also sustain heavy losses from the decimations of the same scourge.

Now it is a very significant fact that precisely in these infected districts, 'malignant pustule' is a common disease. A single German observer, Dr. Nicolai, speaks of having seen no less than three hundred cases. Thus the infrequency of the disease in the British Isles, is to be accounted for by that remarkable immunity from anthrax enjoyed by our domestic animals, to which allusion has previously been made. Moreover, in the cases encountered in English practice, almost invariably the source of infection can be traced to the products of diseased animals imported from abroad.

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* Micro-parasites in Disease (New Sydenham Society), p. 561.

† *Le Charbon et la Vaccination Charbonneuse*, pp. 10, 11.

2. *Association with particular occupations.*—The sufferers are either persons who have to do with dead and living anthracised animals, or who, by reason of their employment in connection with certain industries, are brought into contact with materials derived from such animals,—*ex. gr.* fleeces, hides, skins, hoofs, horns, bones, hair, wool, bristles, flesh, blood. Hence the disease is acquired by shepherds, butchers, farm-labourers, farriers, veterinarians, tanners, curriers, leather workers, wool-sorters, fellmongers, furriers, fur-dyers, workers in horse-hair factories, makers of woollen hats, and dock porters.

A digest of the series of twenty-six cases referred to above (pp. ~~67~~ 1, ~~68~~ 2), as having been treated at Guy's Hospital, affords a striking illustration of this point: fifteen of the patients were tanners, or workers in hides and skins; nine were wharf porters; and one—a woman—was the wife of a stevedore. The remaining case was a girl, aged eleven, who lived in the neighbourhood of tanneries, but the mode of infection was not ascertained.

Moreover, as bearing on the question of the influence of occupation, it is to be noted that women and children are much less often attacked than men. In the districts where anthrax is enzoötic it is estimated that amongst adult patients, 59 per cent. are men. But in non-infected countries, the proportionate number of women patients is considerably lower, the disease being practically restricted to male operatives. Of the Guy's cases upwards of 88 per cent. were men, leaving about 12 per cent. for women, and of these, one—a girl of 14—was employed on Australian rabbit skins, by which she was probably infected. Two of the patients were under 15; the ages of all the rest ranged between seventeen and fifty years, corresponding to the period of working activity.

A characteristic mode of infection, as also the extreme virulence and tenacity of the contagium, are well exemplified by the following narrative of Einike:*—"The skin of an ox (from whose flesh two persons got carbuncle, *i. e.* 'malignant pustule'), which died in the fall of 1852, was soaked in the following spring in the water of a pond, and then made up by a saddler into harness. The saddler got carbuncle. From a flock of sheep which were washed in the pond four weeks later, twenty perished in a few days of anthrax, and both of the horses (for whom the new harness was made), after they had worn it for four days, died of the disease in forty-eight hours."

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* Ziemssen's Cyclopædia of Medicine: article by Bollinger, Vol. iii., p. 394.

Fournier, in 1769, reported on the frequent infection of men engaged in the tapestry works at Montpelier by the wool used in the process of manufacture.

3. *Site of local lesion.*—The so-called 'pustules' are found almost without exception on parts of the body uncovered by the dress, especially the face, neck, and fore-arm. When occurring on surfaces less commonly exposed, as the arm and leg (constituting 16 per cent. of the cases investigated by Virchow), the persons affected habitually leave these parts uncovered.

To refer again to the Guy's Hospital cases, the lesion was situated 15 times on the face, 8 times on the neck, and 3 times on the fore-arm. The explanation is obvious when regard is had to the facilities such places offer for inoculation—as by the direct contact of anthracised materials (hides, etc.), or by scratching pimples and abrasions with fingers charged with the virus, or by flies.

Bollinger says it has been established that anthrax poison can penetrate into the body through the unbroken cuticle, probably by first entering the hair follicle. It is certain that bacteria similar to the *b. anthracis* can pass through such a barrier as egg-shell.

4. *Constant presence of Micro-organism.*—i. *Biology.*—If the blood of an animal suffering from anthrax be examined microscopically shortly before or after death, there will commonly be found immense numbers of delicate, straight, cylindrical rods of extreme tenuity, and having a length, according to Bollinger, of $\frac{1}{3700}$ to $\frac{1}{2000}$ of an inch. Dr. Charlewood Turner * has described specimens obtained from a patient treated by Mr. Davies-Colley, measuring $\frac{1}{1400}$ to $\frac{1}{1600}$ of an inch in length.

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* Medico-Chirurgical Transactions, 1882.

Dr. Greenfield gives $\frac{1}{5000}$ to about $\frac{1}{1600}$ of an inch as the measurements of bacilli from man. These discrepancies are, perhaps, to be accounted for by differences in point of age, or in the quality of the materials in which the micro-organisms were cultivated. The rods have never been seen in motion. They are minute vegetable organisms (fungi), consisting of granular, achlorophyllous protoplasm enclosed in a delicate sheath. They are the bodies first discovered by Pollender in 1849, the 'vibriones' of Brauell, the 'bacteridia' of Davaine, the 'bacilli anthracis' of Cohn.

When observed under favourable conditions the bacillus is seen to quickly elongate, and in its interior, at regular intervals, spherical spores appear. Later, the filaments break up allowing the spores to become free. The spores germinate and develop into bacilli in all respects similar to the original one. The filaments may also multiply by transverse, equidistant subdivisions. The organism can be identified by its want of mobility, the shape of its extremities, its dimensions, and the position of the spores; as well as by its well-marked physiological properties.

In common with all bacteria it requires organic and inorganic nutritive substances,—carbohydrates, albuminoids, sulphur, phosphorus, magnesium and potassium; these must be presented with water. Free oxygen is also necessary to the existence of *b. anthracis*: hence Pasteur terms it an *aërobious* fungus. It develops best at a temperature between 30° and 40° C. (= 86° and 104° F.) The bacilli, and especially the spores, are very tenacious of life: the latter resist exposure to the freezing and boiling temperatures of water, and are only destroyed after three hours in a temperature of 140° C. (284° F.); they may be dried, and in that state preserved for an indefinite time.

Various substances are very inimical to the life of bacilli: an aqueous solution of corrosive sublimate of the strength of 1 : 20,000 kills the spores in ten minutes; iodine and carbolic acid are also effective; "chloride of zinc, however, in a 5 per cent. solution has no effect on anthrax spores, even when they have lain in it for a month" (Koch). Disinfecting agents should be used in aqueous solution, as they are enfeebled in alcohol or oil.

The fully-developed organism is not found in all specimens of anthracised blood; but it has been shewn that spores are present even in the absence of the rods, and that inoculation with such blood may produce true anthrax with filamentous bacteria. Bacilli are also found in sputum, urine, fæces, and sweat.

ii. *Histology of 'Malignant Pustule.'*—Davaine,* in 1863, was the first observer who described the microscopical appearances in the skin. He found numerous bacteria in the focus of the disease.

Viewed *macroscopically* the 'pustule' displays three concentric zones:—(α) a central black eschar; (β) surrounding this, a wreath-like ring of vesicles on a red indurated base; (γ) next, a zone of redness and œdema of varying breadth.

Davaine reported that the organisms were chiefly embedded in the Malpighian layer of the skin beneath the central eschar: here they were grouped together in the form of islands; at the periphery they were scattered between the epithelial cells.

Dr. Charlewood Turner† has given an elaborate histological account of a typical 'pustule' removed during life by Mr. Davies-Colley. Dense aggregations of bacilli were found, especially about the margin of the eschar, just beneath the rete Malpighii. In the situation of a vesicle, the appearance is as though there had been a separation between the cutis and the Malpighian layer above, and that sero-fibrinous exudation escaping into the space so formed, had undergone changes affording conditions specially favourable to the development of the bacilli. Along the sheaths of the hair-follicles the rodlets were numerous; but none were found in the subcutaneous adipose tissue. Here and there the bacilli were studded with spores; others were broken up into short pieces.

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* *Comptes Rendus*, LX., p. 1296.

† Loc. cit. supra.

Mr. Arthur E. Barker* has confirmed and somewhat extended Dr. Turner's observations. He found the bacilli in great abundance beneath the intermediate (vesicular) zone of the 'pustule;' they were also numerous where vesicles were about to form, the apices of the papillæ appearing to be softened and disintegrated by their action; whilst they were comparatively scarce beneath the central eschar. Mr. Barker lays great stress on the superficial distribution of the parasite, its favourite habitat being the apices of the papillæ and the adjacent layers of the rete Malpighii. He associates this fact with the dependence of the bacilli upon air for their functional activity.

iii. *Theory of the action of Bacilli Anthracis.*—The enormous multiplication of the micro-organism in infected blood—as many as ten millions being computed to exist in a single drop—must lead to a considerable consumption of oxygen; and, as there is so little of this gas dissolved in the serum, the conclusion has been drawn that the red corpuscles furnish the supply at the expense of their oxy-hæmoglobin. The lividity and dyspnœa common in fatal cases, have been relied upon as proof by the supporters of this view; and Mr. Bryant† has hereon based the suggestion that gaseous oxygen might be inspired as a therapeutic. But M. Colin‡ denies that there is any relation between the number of germs and the degree of asphyxia. We are disposed to think that the bacilli can obtain their needed oxygen from the respired air, whilst they are passing through the pulmonary circulation, oxygenation of the reduced hæmoglobin being, at the same time, impaired.

Probably, much more dangerous than deficient aëration of the blood, is the production of poisonous chemical substances (ptomaines), at the site of the local lesion, and their subsequent diffusion throughout the body. That such septic products result from the activity of certain organisms in animal bodies, is well known.* Pasteur suggests that there is even such a thing as bacterial suicide, the microbes being injured by their own poisonous productions.†

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* Medico-Chirurgical Transactions, Vol. LXIX.

† Lancet, Mar. 10, 1883: Report of Pathological Society.

‡ Acad. de Méd., Paris, Séance, Nov. 12, 1878.

iv. *The spread of Anthrax.*—The light and almost indestructible spores are the chief agents in propagating the disease. Every part of an infected animal appears to harbour them or the mature bacilli, and they may be transported immense distances by winds, or by commerce; then, if they enter a suitable soil, germination follows.

Enzoötic anthrax is to be accounted for by the faulty disposal of diseased remains. Even after tolerably deep inhumation, it would appear that earthworms can take the germs to the surface, and there deposit them in their castings. Cattle are thus liable to infection while cropping the herbage. Pasteur's views on this point‡ have been opposed by Koch,|| but confirmed by a Commission appointed by the French Academy of Medicine.§ The Commissioners caused the death of a guinea-pig from anthrax, by inoculation with earth taken from a trench wherein infected carcases had been buried twelve years. Earthworms found in this grave contained bacilli in their intestines; and cultivations of the micro-organisms, effected the fatal anthracisation of guinea-pigs.

These facts have an interesting and instructive bearing on the old malarial theories.

5. *Inoculation of Animals with Bacilli Anthracis.*—The allusion to inoculations in the preceding sub-section may serve as a fitting introduction to a more detailed consideration of the experimental evidence bearing on the causal relationship between the germ and the disease.

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* Vide 12th Rep. of Med. Off. to Loc. Gov. Bd., by Dr. Burdon Sanderson.

† Micro-parasites in Disease: New Sydenham Soc., p. 641.

‡ Bulletin de l'Acad. de Méd., 1880.

|| Mittheil. Gesundheit., 1881.

§ Lancet, May 8, 1881.

Pollender, the first discoverer of the bacillus, refrained from committing himself to any definite opinion as to its derivation and significance. Brauell, who made the discovery independently a few years later, formulated the proposition that the bacilli did not constitute the poison of anthrax, nor were they its carriers, though they gave valuable indications for diagnosis and prognosis. He failed to detect the rods in the blood of animals convalescing from anthracæmia, though they were constantly present in the blood of cases about to terminate fatally. By way of experiment* he took blood not displaying the mature organisms, and with it inoculated two foals, producing in them genuine anthrax, their blood yielding on examination abundance of bacilli. This observation, which was corroborated by Bouley and others, appeared to be a destructive argument against the theory of Brauell's contemporary, Davaine, who contended that the germs were the active agents in the propagation of the disease. But this was more than twenty years ago. Improvements in optical apparatus and in laboratory technique have cleared up the disputed points, and vindicated the soundness of Davaine's position. Bollinger,† besides G. W. Müller, Schuster, and others, has demonstrated that infectious blood in which the rods cannot be discovered, nevertheless contains the immature germ in the form of spores.

Klebs showed that filtered blood was innocuous; it may hence be inferred that the virus depends on insoluble concrete particles, and there can be no doubt that these particles are anthrax bacilli or spores. Koch, Klein, Greenfield, Pasteur, and others have isolated the organism, and made cultivations in suitable nutritive media outside the body. The inoculation of the blood of animals with such cultivations produces typical anthrax.

Dr. Greenfield detected the rods in the serum from a 'malignant pustule' on the arm of one of Dr. Bell's Bradford cases, and by inoculation of a guinea-pig with this serum he caused anthracæmia, which proved fatal in fifty-three hours. Numerous confirmatory experiments of a like kind have been published.

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* Virchow's Archiv, B. xxxvi., 1866 † Zur. pathol. des Milzbrandes, p. 48.

Koch finds that there are marked differences in susceptibility to the poison amongst different animals. In guinea-pigs the bacilli propagate freely—so much so that the number of rods may exceed the number of corpuscles; rabbits are less susceptible; and mice still less so; whilst dogs, and the carnivora generally, are peculiarly refractory to the germ. Man also, does not readily yield to infection.

In summing up the evidence relating to inoculation, it may be safely asserted that, given a susceptible animal, and true anthrax bacilli or spores, the successful inoculation of the blood of the animal with such germs will certainly be followed after a brief incubation by an attack of genuine anthrax.

6. *Infection by the agency of Insects and by Diseased Food.*—Montfils (1776) declared that anthrax was communicated to man by the bites of flies. Davaine and Raimbert have established experimentally that the proboscis, feet, and dejections of the common house-fly, and, of the blue-bottle, serve as efficient vehicles for the transmission of the disease.

Bollinger* found the organisms in the stomach and intestines of horse-flies collected from the body of a steer dead of anthrax, and, by inoculation, he communicated the disease to two rabbits.

Infection, by eating diseased food stuffs is not common. In this respect man resembles the carnivora, though insusceptibility is not so complete as in the latter. It is alleged that milk and butter from diseased animals possess virulent properties.

Professor James Law of Cornell University, U.S.A., asserts† that animals have perished after licking frozen anthracic blood.

Cooking the food does not always destroy the germs.

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* Ziemssen's Cyclopædia of Medicine, Vol. III., p. 383.

† Report to American National Board of Health, 1880.

III. CLINICAL.

The third and concluding division of the paper will be devoted to the consideration of the clinical features of 'malignant pustule,' embracing its symptomatology, differential diagnosis, treatment, and prognosis, each of which will be briefly discussed. Finally, an illustrative case will be reported.

1. *Symptoms.*—i. *Local.*—Following inoculation of the skin with the virus, there is a period of incubation, usually of several days' duration, but varying from a few hours to fourteen days. Then there appears on the spot a red speck with a dark centre, like a fleabite: this may be preceded or accompanied by more or less itching.

Within twelve or fifteen hours a papule capped with a small vesicle forms, and gradually enlarges. The vesicle soon bursts, as a result of increasing distension or scratching, disclosing in its floor a brownish patch of skin, which speedily becomes a black, dry eschar. The surrounding integument meanwhile swells and reddens, and in less than twenty-four hours is studded with a crop of vesicles each as large as a hemp-seed.

The appearance is now highly characteristic: there is a central depressed, black eschar, somewhat less in diameter than a three-penny-bit, encircled by a wreath of yellowish vesicles on a tumid, inflamed base, quickly merging into healthy skin. Thus are produced the three zones mentioned above (p. 13 ~~121~~). As the gangrene spreads centrifugally the first ring of vesicles falls into the eschar, and another series develops. By the third or fourth day, swelling and œdema have extended for a considerable distance from the inflamed focus, which now feels hard and solid, constituting what the French have designated the *bouton.* The adjacent lymphatic glands become enlarged and tender, the lymph vessels leading to them showing as red lines.

The eschar rarely increases beyond the size of a florin (it is usually more or less circular in outline); frequently it is not larger than a split-pea. In thickness the eschar is not considerable, being limited by the true skin.

The vesicles discharge an abundance of clear, straw-colored, or reddish *serum*, but no *pus;* indeed, it is a remarkable and diagnostic feature that no pus appears until the eschar begins to slough out. This event occurs in favourable cases in a fortnight or three weeks. The writer has seen the serous exudation from the vesicular zone run in a slow stream down the cheek and drip over the border, reminding one of what is observed when a nine-days-old vaccine vesicle is punctured.

It is noteworthy that throughout there is little or no severe pain, and that the temperature of the part is usually but slightly raised.

ii. *Constitutional.*—An early subjective symptom is chilliness followed by rigors and headache, with, not uncommonly, retching and vomiting. Muscular debility ensues, and this is associated with feelings of wretchedness and depression of spirits. Pyrexia is not, speaking generally, a prominent symptom, and is often absent. It will be seen, therefore, that in the early stages of an ordinary case, the general condition does not betoken the gravity of the disease, and hence patients are apt to continue at their occupation without seeking advice.

In unfavourable cases, urgent dyspnœa causes great alarm and distress; cyanosis is then an attendant symptom, and sometimes cough. Or there are cold sweats, diarrhœa and collapse; the chief stress of the poison falling upon the intestines rather than the lungs.

In yet another group of cases, septicæmic symptoms are conspicuous. The temperature is high, but is subject to fluctuations, and different records are obtained in the axilla, mouth and rectum; there are exhausting sweatings, diarrhœa, and severe pains in the limbs; the pulse and respirations are hurried; and confusion, delirium, and occasionally clonic spasms, usher in a fatal termination. In these cases secondary anthrax nodules are usually found *post mortem* in the stomach, intestines and lungs; together with hæmorrhages in the mesenteric glands, meninges of brain, and elsewhere; the spleen is large and often diffluent; the blood is tarry, abnormally fluid, and with the hæmoglobin of the red corpuscles in partial solution.

In fatal cases, death takes place in from four to eight days from the onset of constitutional symptoms.

2. *Differential Diagnosis.*—i. *From Malignant Carbuncle of the Face.*—In this there are usually yellow spots of suppuration here and there on the inflamed part; the pain is severe; constitutional symptoms are early and grave; the adjacent veins are implicated; and the characteristic eschar and vesicles are absent. Further, the necrosis advances to the surface from below, instead of spreading superficially.

ii. *From Glanders.*—Here the cutaneous lesions are multiple pustules or pemphigus blebs; the nasal mucous membrane is commonly implicated; and there is a history of infection from a horse.

iii. *From Simple Poisoned Wound.*—This usually presents one large, painful pustule, or an angry-looking focus, whence the red cords of lymphangitis pass to enlarged and tender glands. The vesicles are conspicuously absent.

iv. *From Noma.*—This begins on mucous membrane, commonly of the mouth; it is associated with a zymotic disease such as measles, and with profound cachexia and extreme pallor; the sloughs are more extensive, and withal, soft and very foul.

v. *From Primary Syphilitic Chancre* the diagnosis is not always easy, for here a large scab is formed on a red, indurated base, and the soft parts and contiguous glands are swollen. The pain, however, is usually considerable, while the development is slow. In 'malignant pustule,' the comparative painlessness of the swelling, and the occupation of the patient are points of importance. Lastly, in this, as in all other cases where the diagnostician is likely to be puzzled, the absence of bacilli or spores on microscopical examination will help to resolve the doubt.

3. *Treatment.*—When once the nature of the disease is understood, the indications for treatment appear obvious. The local infection, and the definite localization of the malady in the early stage, clearly demand a local remedy. And this must be applied promptly and thoroughly if it is to be effectual. After an interval of time, longer or shorter, the limits of the virus become coterminous with the organs of blood-circulation, and then recovery must as a rule be despaired of. In one word, then, the principle of treatment is destruction or removal of the local lesion. At Guy's Hospital very satisfactory results are yielded by excising the affected piece of skin with the knife, cutting at least a quarter of an inch outside the vesicular zone, and as deep as the subcutaneous fat, some of which is also removed. The bleeding surface is then variously treated by the different surgeons, one or other of the following escharotics being used:—caustic potash, pure phenol, nitric acid, zinc chloride, and Pacquelin's *thérmo-cautère.* After the bleeding has been checked, any simple dressing may be applied.

No doubt other forms of destruction may succeed, as for example, the application of caustics after preliminary incisions; but these methods cannot be relied on with the confidence attaching to the one advocated. Bourgeois recommends caustic potash; but in spite of the use of this remedy, in some of his cases the disease appears to have spread.

The 'Dallack' doctors of Constantinople have a great reputation for curing the malady, their routine treatment being excision or actual cauterization.

It is encouraging to remember that energetic destruction of the primary focus often proves successful even when the adjacent glands are affected, and symptoms of toxæmia exist. It would seem, therefore, that at least the chief source of the actual virus is within or immediately around the 'malignant pustule' itself; and that the system can eliminate a certain amount, providing the supply is not maintained.

In suitable cases internal remedies may be exhibited with great advantage. Thus where symptoms of blood-poisoning are present, quinine and carbolic acid are indicated, and may be given to the extent of forty grains of the former, or ten of the latter *per diem.* Preparations of mercury are also valuable. Diffusible stimulants, as ammonia, alcohol, and ether, must be used according to the requirements of the particular case.

With regard to diet some very important and interesting information has been gleaned. Mr. Spier, in his observations on the cases amongst the Bradford woolsorters,* calls attention to the apparent aggravation of symptoms after the ingestion of vegetable food-stuffs. He was led to conclude that the consumption of such aliments greatly favoured the development of bacilli. It is remarkable that the Turkish 'Dallack' doctors prescribe a diet of caviare and bread, and a little spirit, vegetables and fruit being considered specially dangerous.

In this connection the experiments of Prof. Feser of Munich, are significant. He found that rats fed exclusively with beef and horse-flesh could not be inoculated with anthrax; whereas others fed only with bread could be inoculated with ease.

These facts coincide with the well-known insusceptibility of the carnivora.

As to prophylactic inoculation, little need be said. The *odium pathologicum* which has been imported into the discussion, makes it the less inviting, and in any case it is much more a Continental than an English question. It would be clearly undesirable to introduce the virus of anthrax into a country which at present enjoys comparative immunity. On the whole the weight of evidence certainly proves that the inoculation of animals with attenuated cultures of the bacillus, confers at least a temporary immunity.†

4. *Prognosis.*—It is difficult to collect reliable statistics as to the occurrence and fatality of 'malignant pustule,' inasmuch as

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* Report of Medical Officer to Local Government Board, 1881.

† Micro-parasites in Disease: New Syd. Soc., pp. 572, 575.

cases are so frequently not diagnosed. Bollinger estimates the mortality at not less than 30 or 40 per cent. Under efficient treatment, however, much better results are obtained. Nicolai lost only 11 out of 209 patients, *i.e.* 5 per cent. There are few diseases in which so much depends on sound diagnosis and treatment. Provided bold measures are adopted before profound constitutional symptoms declare themselves, the prognosis is decidedly good. In the series of Guy's Hospital patients, out of 24 treated by excision, 21 recovered.

CLINICAL REPORT OF A CASE.

The case which is here narrated came under the writer's close observation during his house-surgeoncy at Guy's Hospital, and he is indebted to the kindness of his former teacher, Mr. H. G. Howse, for permission to publish the notes.

Edward W., æt. 37, was admitted into Naaman Ward under Mr. Howse, on 28th July, 1883. He is employed at a warehouse for dry hides in Bermondsey; a fellow-workman died of 'malignant pustule' in Guy's Hospital last February. Ten years ago he was a hard drinker; about that time he had an attack of lead-poisoning. Of late he has been very steady, and his general health has been excellent. He is married and has five children.

History of Present Disease.—On 23rd July, patient noticed a pimple on his right cheek; at first it caused no pain; but by the 27th it had got larger and 'burned.' Clear discharge began to ooze on the morning of admission. The only treatment has been bathing with warm water.

Condition on Admission.—He is a healthy-looking man; says he has no pain. On the right cheek in a line from meatus of ear to angle of mouth is a swollen patch of skin raised about one-tenth of an inch above the general surface, and measuring half-an-inch across. It presents a black, dry eschar one-eighth of an inch in diameter, having a slightly depressed centre and raised edge, from beneath which clear serum is oozing and searing the cheek. Surrounding the eschar is an area of vesication, as of one large annular vesicle.

Outside this the skin is dark-red in colour, and hard to the feel; the outermost zone is swollen and infiltrated, though not positively brawny; this is bounded by a line drawn through meatus of right ear, running below jaw for about two inches, thence up to angle of mouth, onward to right nostril, and back to right outer canthus. There are three enlarged, tender glands beneath jaw.

Tongue red at edges, furred in the middle. Bowels were open loosely at 6-30 a.m. to-day; he frequently has a kind of diarrhœa. Pulse and respiration normal.

July 28. *Operation at 10 a.m. under chloroform.* The 'pustule' was excised down to the subcutaneous fat, the incision passing a quarter of an inch wide of the raised patch all round. The bleeding surface was rubbed over with a stick of caustic potash. Carbolic gauze dressing was applied, and the patient removed to bed.

July 29. Dressed: slight sero-sanguineous discharge. Ordered Pil. Col. c. Cal. gr. x., h.s.s., and Haust Sennæ ʒ iss. cras mane. To take milk and ice.

July 30. Very comfortable. Low diet.

Aug. 2. Going on well. Rep. Pil. Aper. Middle diet.

Aug. 3. Wound granulating healthily. General health very good.

Aug. 5. Got up to-day.

Aug. 16. Has been steadily convalescing; wound covered with healthy granulations, and has a healing edge; dressed with Ung. Resinæ. General health excellent. Discharged 'cured.'

		Temp.
July 28	M.	98·4
	E.	98
July 29	M.	98·2
	E.	100·6
July 30	M.	99
	E.	98·8
July 31	M.	98
	E.	98
Ang.. 1	M.	98
	E.	99
Aug. 2.		98·8
Aug. 3.		98
Aug. 4.		98

In conclusion it should be mentioned that ordinary *bacilli anthracis* were found on microscopical examination of the excised skin.

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